

Amendments to the Specification:

Please replace paragraph [0026] beginning at page 6, line 14, with the following:

--[0026] **Figure 10** illustrates a hairpin structure (SEQ ID NO:1) simulating a probe-target nucleic acid-enhancer complex as a model substrate for an AP endonuclease. Cleavage of this substrate in reaction with *E. coli* endonuclease IV is also shown on Figure 10. The reaction was monitored as fluorescence vs. time in 5 mM MgCl₂, 20 mM Tris-HCl (pH8.5). Experiment was performed on ABI PRISM™ 7700 Sequence Detector at 60 °C with the hairpin substrate concentration of 150 nM and the enzyme concentration of 0.0004 U/μL. Structure of the tail used in this example is shown in Figure 7, structure #2.--

Please replace paragraph [0097] beginning at page 27, line 3, with the following:

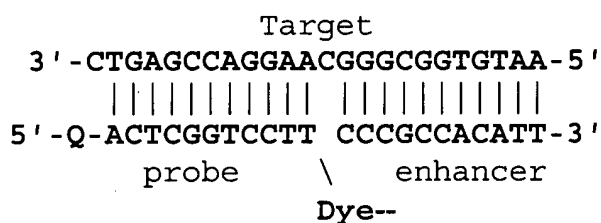
--[0097] In preferred embodiments, a probe-enhancer linker is comprised of individual or combined repeats of substituted alkyl backbone moieties, including (-OCH₂CH₂)_n, (-OCH₂CH₂-OPO₂)_n or -O(CH₂)_nO-. Typically, n is from 1-100, more typically n is 10, 20, 40, 50, 60 or 80. In other embodiments, a linker is a flexible polypeptide chain, for instance, dihydropyrroloindole peptides or a series of one or more repeats of a Gly-(Ser)₄ (SEQ ID NO:2) polypeptide sequence. In another embodiment, the linker is an oligonucleotide, such as poly A or poly T and the like. In yet another embodiment, the linker is an alkyl chain having a backbone typically of about 100, 200 or 300 atoms, more typically of about 40, 60 or 80 atoms. Other alkyl linkers of potential use are described in U.S. Patent Publication No. 2003/0113765, incorporated herein by reference. Additional linkers that may find use are described by Dempey, *et al.*, *Nucleic Acids Res.* 27:2931 (1999); Lukhtanov, *et al.*, *Nucleic Acids Res.* 25:5077 (1997); Lukhtanov, *et al.*, *Bioconjug. Chem.* 7:564 (1996); and Lukhtanov, *et al.*, *Bioconjug. Chem.* 6:418 (1995). Appropriate linkers can be obtained from commercially available sources, for example from Pierce Biotechnology, Rockford IL (www.piercenet.com/). Guidance for selecting an

appropriate linker for attaching oligonucleotides is provided in Haugland, *Handbook of Fluorescent Probes and Research Products, supra*. These linkers also find application in attaching an AP site probe or an enhancer to a solid support.--

Please replace paragraph [0110] beginning at page 27, line 3, with the following:

--[0110] This Example demonstrates the efficacy of an Endonuclease (Class II AP endonuclease) tail-cleavage assay.

Assay design and oligonucleotide component structures (SEQ ID NOS:3-5):



Please replace paragraph [0115] beginning at page 33, line 7, with the following:

--[0115] This Example illustrates that the efficiency of the AP endonuclease tail-cleavage reaction depends on the balance between the hybridization properties of the probes and temperature of the reaction. Probes complementary to target of 11, 9, 7 and 6 nucleic acids in length were prepared.

Assay design, component structures (SEQ ID NOS:3-5) and melting temperatures (T_m):

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                                target
                                3' -CTGAGCCAGGAACGGGCGGTGTAA-5'
                                |||||
11-mer probe ( $T_m$ = 45°C)    5' -Q-ACTCGGTCCTT CCGCCACATT-3'
                                \ enhancer ( $T_m$ = 50°C)
                                FAM
9-mer probe ( $T_m$ = 35°C)    5' -Q-TCGGTCCTT-FAM
7-mer probe ( $T_m$ = 19°C)    5' -Q-GGTCCTT-FAM
6-mer probe ( $T_m$ = 2°C)     5' -Q-GTCCTT-FAM
Base-Modified 6-mer probe ( $T_m$ = 13°C)--

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Please replace paragraph [0118] beginning at page 34, line 13, with the following:

--[0118] This Example illustrates the substrate specificity of *E.coli* Endonuclease IV. In this set of experiments (SEQ ID NOS:3-7), the enhancer was positioned along the target sequence to provide a gap between the duplexes of the probe and enhancer of 0, 1 or 2 nucleotides.

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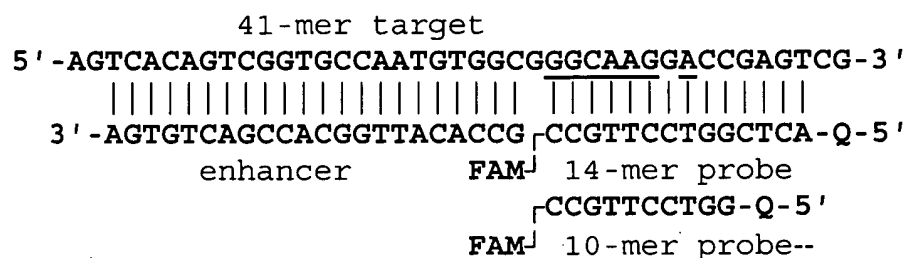
                                target
                                3' -CTGAGCCAGGAACGGGCGGTGTAA-5'
                                |||||
5' -Q-ACTCGGTCCTT CCGCCACATT-3'
                                \
                                probe      enhancer for 1 base gap ( $T_m$ = 50 °C)
                                FAM
                                5' -GCCCGCCACAT-3'    enhancer for 0 base gap (SEQ ID NO:6)
                                5' -CCGCCACATT-3'     enhancer for 2 base gap (SEQ ID NO:7)--

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Please replace paragraph [0122] beginning at page 35, line 11, with the following:

--[0122] This Example illustrates the application of the tail cleaving assay to the discrimination of single base pair mismatch. Endonuclease IV discriminates single base-pair mismatches, particularly those located at the 3'-end of AP site probe hybridized with a target nucleic acid.

Assay design and oligonucleotide component structures (SEQ ID NOS:8-11):



Please replace paragraph [0128] beginning at page 37, line 14, with the following:

--[0128] A fragment of the target sequence around the polymorphism is shown above (SEQ ID NO:12). The T/C mismatch is underlined. First and second probe were labeled with a fluorescent tails that are shown on Figure 7, structure #8 (FAM) and #7 (YD) respectively. Q is a 5'-conjugated quencher (structure #15) shown on Figure 8. The A and T bases are substituted with modified bases "a" and "t".--

Please replace paragraph [0129] beginning at page 37, line 19, with the following:

--[0129] Three individual samples of the human genomic DNA that were prior genotyped as T-homozygous, T/C-heterozygous and C-homozygous at the polymorphism of interest were amplified in an asymmetric PCR. PCR were performed on ABI PRISM™ 7700 Sequence Detector using forward CAAACTTTGTCCTTGGTCTA (SEQ ID NO:13) and reverse TTCTTTTACCACTCCCCCTT (SEQ ID NO:14) primers and a PCR cycling profile: 2min50°-2min95°-(5sec95°-20sec56°-30sec76°)x50 times.--

Please replace paragraph [0132] beginning at page 38, line 9, with the following:

--[0132] This Example illustrates that cleavage of a functional tail **R** from an AP site probe does not effect on the probe hybridization properties. Two samples were prepared by mixing a complementary target oligodeoxyribonucleotide 5'-CAAGGACCGAGTC-3' (SEQ ID NO:15) in 5 mM MgCl₂, 20 mM Tris-HCl (pH8.5) with ODN probes 5'-**Q**-ACTCGGTCCTT-**FAM**-3' (SEQ ID NO:16) and 5'-**Q**-ACTCGGTCCTT-3' (SEQ ID NO:17), respectively. **Q** is a 5'-conjugated quencher (structure #15) shown on Figure 8. **FAM** is an endonuclease cleavable tail comprising of a fluorescein dye and linker that are shown on Figure 7 (Structure 8). Denaturation profiles of the duplexes are shown on Figure 17. These profiles were obtained by monitoring the sample absorbance (A_{260}) vs. temperature (0.4 °C/min). The target ODN was taken in 1.2 fold excess over the probes that were at 1 μ M concentration.--

Please insert the accompanying paper copy of the Sequence Listing, page numbers 1-6, at the end of the application.